sics, suggesting a role of these latter compounds in the progression to ESRD in AAN.

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To the Editor: The article in the December 2000 issue of *Kidney International* by the Ad Hoc Committee of the International Study Group on Analgesics and Nephropathy [1] questions the harmful impact of nonphenacetin-containing analgesic mixtures on the kidneys. We wonder whether there is a need for these combinations at all. APC brands have never been proven to be effective for the indication of chronic pain treatment. The introduction of these formulations is based on an irrational guiding principle presented by Buergi in 1927 (references in [2]). The German view is (*1*) almost none of the single analgesics (not even phenacetin) have been taken regularly in amounts reached by mixed compounds; and (*2*) since over-the-counter analgesic compounds have never been sold without caffeine (20 to 50 mg per unit) and since low-dose caffeine alone is not effective for pain relief (with the exception of caffeine-withdrawal–induced headache), why is it still used?

Our study provides evidence that, besides phenacetin, paracetamol-containing mixtures do increase the risk of end-stage renal disease [3]. Because risk estimates are based on hospital controls, the specific risks for the general population may be even higher. Detrimental renal effects of high-dose paracetamol exposure are well documented in both clinical and experimental studies [summarized in 4, 5].

Warnings about the adverse effects of phenacetin and nonphenacetin-containing compounds have been ignored for a long time [6]. The debate continues, why and for what?

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Reply from the authors

The letters from Nanra and Lornoy et al claim that the incidence of analgesic nephropathy (AN) would be controlled not by an isolated phenacetin withdrawal, but by a ban on all combined analgesics. Nanra's conclusion, however, was based on short-term observations in a limited number of patients [1]. In Australia, phenacetin was progressively withdrawn from the abused brands of analgesics, and its sale was legally prohibited in 1977. Two years later, the sales of all combined analgesics were also restricted. Because the renal consequences of phenacetin may not occur until many years after intake has ceased, the limited follow-up after phenacetin withdrawal alone does not allow its effects to be separated from those of the later withdrawal of combined analgesics. Theoretical speculations, such as those about the toxicity of paracetamol, can only suggest hypotheses. All the proposed hypotheses, however, should be (but have not been) compatible with the evidence that the incidence of AN decreased similarly, in both Belgium and Australia, despite persistently high consumption of mixed nonphenacetin analgesics in Belgium [2, 3].

Lornoy et al state that the incidence of AN in their dialysis unit correlated better with the withdrawal of nonphenacetin analgesics than with the withdrawal of phenacetin. Because AN is not evenly distributed by geographic region, however, local incidence data are influenced by changes in recruitment of patients for dialysis due to a changing pattern of referral by local nephrologists and/or to the opening of new regional dialysis units. The data in the figure by Lornoy et al do not show the expected progressive increase in the total number of patients admitted for dialysis and are most consistent with a change